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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,992	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-46 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 18 July 2005 in response to the Non-Final Office Action mailed 18 January 2005. Claims 42-46 and 49-51 were considered in the 18 January Office Action. No claim amendments were filed with the 18 July Paper. Claims 42-46 and 49-51 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Change of Address

Receipt of the change of address filed 4 March 2003 is acknowledged.

Response to Arguments

Claim Rejections - 35 USC § 101 and 112, first paragraph

Claims 42-46 and 49-51 **stand rejected** under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for reasons of record and herein below.

Response to Arguments

In response to the *prima facie case*, set forth in the Office Action mailed 26 February 2003, and arguments of record Applicant first provides a general summary of the utility standard. It is noted that the summary quotes from MPEP §2107 II (B)(1) as follows, "If the (A)pplicant

has asserted that the claimed invention is useful for any particular practical purpose... and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." The phrase omitted by Applicant reads as follows "(*i.e.*, it has a specific and substantial utility)". As repeatedly stated throughout prosecution of the instant application, the issue at hand is whether a "specific" and "substantial" utility has been asserted in the application or would be readily apparent to the skilled artisan based on the disclosure of the invention. The complete passage clearly indicates that a rejection should not be imposed only if the asserted utility is both "specific" and "substantial", which requirement is clearly stated in the paragraph that immediately follows the paragraph cited by Applicant.

Applicant's subsequent arguments are directed to the showings of the Rule 1.132 Declaration filed with the 18 July Paper.

Declaration of Sherman Fong, Ph.D. under 37 CFR §1.132

Declarant first cites Miles *et al.*, which is submitted as Exhibit A as teaching the skin vascular permeability assay, disclosed in the instant application as Assay #64, and asserts that the assay has been reliably used for identifying proinflammatory molecules (Paragraph 6).

In Paragraph 7, Applicant states that proinflammatory molecules can directly or indirectly cause vascular permeability, which provides for extravasation of leukocytes at a site of infection or injury (illustrated in Exhibit B).

In paragraph 8, Declarant states that proinflammatory molecules are useful in treating infections, as local administration would stimulate and attract immune cells to the cite of

infection. Declarant cites MIP-1 and MIP-2 as molecules that induce neutrophils to extravasate, CXC chemokines as activators of neutrophils and non-CXC chemokines as chemotactic agents for T lymphocytes. Declarant further states that inappropriate expression of proinflammatory molecules may cause an abnormal immune cell response and leading to tissue destruction and cites various examples of abnormal immune cell responses. Still further, Declarant states that proinflammatory molecules with angiostatic properties are useful in inhibition of angiogenesis in abnormal wound healing, abnormal inflammation or abnormal neovascularization.

In paragraph 9, Declarant states that Miles *et al.* (Exhibit A) used the skin vascular permeability assay to identify proinflammatory and immune related molecules.

In paragraph 10, Declarant states that the skin vascular permeability assay was used in the clinic in determining if factor XIII could be used to treat an immunovascular disease by determining if factor XIII could inhibit vascular permeability induced by anti-endothelial cell antibodies.

In paragraph 11, Declarant states that the skin vascular permeability assay was used to identify VPF (VEGF).

In paragraph 13, Declarant states that the skin vascular permeability assay was performed using purified PRO polypeptide and cites Exhibit I as an example of positive results from a PRO polypeptide.

In paragraph 14, Declarant states the opinion that the PRO polypeptide that shows activity in the skin vascular permeability assay has specific and substantial utility. Declarant states, "examples of utilities include, enhancing immune cell recruitment to sites of injury or infection, or inhibitors to treat autoimmune diseases such as psoriasis *etc.* as discussed above.

Furthermore, the angiogenic or angiostatic properties of proinflammatory molecules would also find practical utility in controlling tumorigenesis."

In the arguments beginning on page 6, Applicant submits that the skin vascular permeability assay (#64) discussed in the Declaration is the same as the vascular leakage assay (#51) for which PRO302 (the claimed polypeptide) was identified as positive except that Assay #64 is followed up with a biopsy. Applicant contends that when one measures vascular "Permeability" versus "Leak" with these assays, one is measuring exactly the same proinflammatory activity. Applicant submits that utilities for PRO302 molecule based on a positive score in the skin vascular permeability assay, such as to treat inflammatory diseases like autoimmune disease, psoriasis, *etc.* are discussed in the Declaration and would be readily understood, appreciated and accepted by those of skill in the art as specific and substantial utilities.

The showings of the Declaration and Applicant's arguments have been fully considered but are not deemed persuasive. It is first noted that the Declaration does not contain any data specific to the claimed PRO302 polypeptide. Instead, the declaration refers to, and presents data from an unidentified "PRO polypeptide". Furthermore, it is noted that the biopsy in Assay #64 "is evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation are scored as positive. Inflammatory cells may be neutrophilic, eosinophilic, monocytic or lymphocytic. At least minimal perivascular infiltrate at the injection site is scored as positive, no infiltrate at the site of injection is scored as negative" (specification, page 210,

lines 34-37). Still further, it is noted that PRO302 is not listed among the polypeptides scored as positive in the skin vascular permeability assay (bridging pages 210-211).

In contrast to Assay #64, Assay #51 does not involve assessment of the injection sites for immune cell infiltrates, which would seem critical to determining whether the polypeptide is a proinflammatory molecule. This is evidenced by the stated purpose of each assay. The specification states, "[t]his assay [Assay 51] is designed to determine whether PRO polypeptides of the present invention show the ability to induce vascular permeability" (page 215, lines 30-31) and "[t]his assay [Assay 64] shows that certain polypeptides of the invention stimulate an immune response and induce inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal" (page 210, lines 23-24). Clearly, if the only difference between the assays is the biopsy, then the biopsy is critical to determining stimulation of an immune response and induction of inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection. Additional evidence that a positive result in Assay #51 does not establish that a molecule has proinflammatory activity is that VEGF is used as a positive control in the assay. VEGF is not known in the art as a proinflammatory molecule (See *e.g.*, Swiss-Prot entry P15692; especially the "FUNCTION" section under the "Comments" heading).

Viewed as a whole, it is clear that a positive result in the Assay #51 indicates that a molecule might or might not have proinflammatory activity and the biopsy in Assay #64 is used to distinguish between these possibilities. The skilled artisan would view the fact that PRO302 is not listed among the polypeptides that were positive in Assay #64 as indicating either that PRO302 was tested and determined to be negative or that PRO302 was not tested in Assay #64.

If the former is the case, clearly Applicant's and Declarant's assertion that the claimed invention can be used to treat inflammatory diseases is groundless. If the latter is the case, then additional experimentation is required to reasonably establish that PRO302 has proinflammatory activity.

It is further noted that, even if the declaration had included data demonstrating that PRO302 has proinflammatory activity, Applicant cannot rely on data that was not available to the skilled artisan at the time of filing to support a well-established utility.

> "If an application fails to disclose one specific, substantial, and credible utility, and the examiner discerns no well-established utility, the examiner will reject the claim under section 101.The rejection shifts the burden to the applicant to show that the examiner erred, or that a well-established utility would have been readily apparent to one of skill in the art. The applicant cannot rebut the rejection by relying on a utility that would not have been readily apparent at the time the application was filed. See, e.g., In re Wright, 999 F.2d 1557, 1562–63, 27USPQ2d 1510, 1514 (Fed. Cir. 1993)('developments occurring after the filing date of an application are of no significance regarding what one skilled in the art believed as of the filing date')." MPEP Federal Register / Vol. 66, No. 4 / Friday, January 5, 2001 / Notices at page 1095, bridging columns 1-2.

Next, Applicant submits that the art available at the time of filing show that the knowledge for vascular permeability factors was well correlated with diseases where "vascular leakage" is an issue. Applicant cites Dvorak as disclosing a vascular permeability factor (now known as VEGF) secreted by hepatocarcinoma cells, which was asserted to be useful for treating tumors. Applicant cites Connolly as showing that the same vascular permeability factor could stimulate endothelial cell growth and Olander as teaching methods of producing antibodies against Dvorak's VPF. Applicant contends that "a positive result in a Miles assay was considered adequate since the art disclosed readily apparent utilities for vascular permeability factors in diseases which included, but were not limited to, angiogenesis, wound healing, burns, antibodies to treat tumor growth, endothelial cells growth *etc.*" (bridging pages 7-8).

Applicant urges, "[b]ased on the 'well-established' utilities for vascular permeability factors in the art as a whole, one skilled in the art would know how to use PRO302 (polypeptides and nucleic acids thereof), or anti-PRO302 antagonists (antibodies) to stop vascular leakage, capillary leakage, tumor leakage, or in burns...Applicants further submit that PRO302's utility lies in its use as a target for the development of anti-vascular leakage agents" (first full paragraph on page 8). Applicant cites *Fujikawa v. Wattanasin* (CA FC) 39 USPQ2d 1895 (8/28/1996) and contends that a rigorous correlation need not be shown in order to establish a practical utility and that, based on positive results for PRO302 in the well-established vascular permeability assay a nexus between PRO302 and "usefulness in disease" has been made.

These arguments have been fully considered but are not deemed persuasive. First, Applicant is reminded that each patent application must be examined on its own merits and the allowance of similar claims to others is immaterial to the allowability of the instant claims (see *In re Giolito*, 530 F.2d 397, 188 U.S.P.Q. 645 (C.C.P.A. 1976). The determination that the instant claims lack specific and substantial utility has been made based on the properties disclosed for the claimed invention in the instant specification, the art available at the time of filing and the Utility Guidelines published January 5, 2001 (*supra*).

Nevertheless, it is worth noting that the properties of the vascular permeability factor disclosed in the Dvorak *et al.*, Connolly *et al.* and Olander *et al.* patents is not limited to the ability of the exogenously added polypeptide to induce vascular permeability. In particular, Dvorak *et al.* establishes that the vascular permeability factor disclosed therein is secreted by tumors and antibodies raised against the vascular permeability factor were found to inhibit vascular permeability induced by tumor cells (see especially Examples 6, 7 and 10) and, as

Applicant points out, Connolly teaches that the vascular permeability factor stimulates endothelial cell growth. Thus, the cited art does not support Applicant's contention that a positive result in the Miles assay alone was sufficient to support a well-established utility for a polypeptide. In contrast to the teachings of Dvorak *et al.*, and as repeatedly pointed out by the Examiner in previous Office Actions, there is no evidence that the claimed PRO302 polypeptide has any role in naturally occurring pathology. Unlike the vascular permeability factor of Dvorak *et al.* there is no evidence that the instant protein is secreted by tumors; therefore, the utility of the invention or reagents developed therewith to treat tumors would have to be established experimentally. Likewise, there is no evidence that the PRO302 polypeptide is in any way responsible for vascular leakage associated with pathological states such as tumors or burns such that the utility of anti-PRO302 antagonists to stop vascular leakage or the utility of PRO302 as a target for the development of anti-vascular leakage agents is established.

As stated in the Advisory Action mailed 16 March 2004, "[t]he skilled artisan would still have had to confirm that PRO302 plays some role in vascular physiology as part of its normal functions in the body in order to demonstrate a substantial utility for the protein in identifying antagonists of this particular activity. One cannot consider that developing antagonists to a protein that may only be involved in disrupting vascular integrity upon injection in large quantities under the skin, a completely artificial situation, as a 'real world' application in and of itself" (page 4, lines 1-7). For example, it would not be surprising to find that the digestive enzyme trypsin disrupted vascular integrity upon injection in large quantities under the skin in view of its ability to disrupt basement membranes of adherent cells in culture. However, one

would not expect that inhibitors of trypsin would have any therapeutic effect in treating tumors or burns because the enzyme is not present in tumors or burns.

With regard to the case law cited by Applicant, the question before the Court in *Fujikawa v. Wattanasin* was whether *in vitro* data presented for a claimed compound reasonably supported similar activity *in vivo*. The Court found, based on the facts in that case, that the *in vitro* data were reasonably correlative. In the opinion, the Court states, "each case of practical utility must be considered on its own facts" (at page 1899) and "there must be a sufficient correlation between the tests and an asserted pharmacological activity so as to convince those skilled in the art, to a reasonable probability, that the novel compound will exhibit the asserted pharmacological behavior" (at page 1899). For reasons of record and herein above, in the instant case there is not sufficient correlation between the tests and an asserted pharmacological activity so as to convince those skilled in the art, to a reasonable probability, that the novel compound will exhibit the asserted pharmacological behavior.

Next, Applicant asserts that the absence of actual data showing the magnitude of the response to PRO302 is not relevant to the determination of whether the invention has a well-established utility. Applicant contends that it is sufficient that Applicant's have asserted that the measured difference was significant to establish that the molecule causes vascular leak and to identify therapies to stop vascular leakage.

This argument has been fully considered but is not deemed persuasive. Even if one were to accept, *arguendo*, that the disclosure is sufficient to establish that PRO302, when injected in large quantities under the skin, induces a significant degree of vascular leakage, the utility of the PRO302 polypeptide remains to be established. Throughout prosecution applicant has variously

asserted that PRO302 is useful because it might play a role in pathologies associated with tumors or burns, might play a role in extravasation of T cells or might have proinflammatory properties useful in treating infections. However, given the disclosed properties of the PRO302 polypeptides, which amount to an assertion that various portions of PRO302 have significant homology with various protease proteins (page 110, top paragraph), although exactly which portions of which other known proteases is not taught, and a statement that PRO302 tested positive in a Guinea pig vascular leak assay (page 216, line 7), the skilled artisan simply would not know which, if any, of these utilities are true. Therefore, no specific and substantial utility would be readily apparent to the skilled artisan based on the disclosed properties of the claimed invention.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §101, as lacking a specific and substantial utility.

Claims 42-46 and 49-51 also **stand rejected** under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph, enablement

Claims 42-46 and 49-51 **stand rejected** under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record and herein below.

The enablement rejection is provided in the event that the rejection outlined above under 35 U.S.C. 101 for lack of a specific and substantial or well-established utility is overcome. The *prima facie* case set forth in the 26 February Office Action finds while it may be possible that applicants can demonstrate that the instant specification and/or prior art provides a specific and substantial or well-established utility for the claimed proteins, there remain other grounds for rejecting the instant claims under 35 U.S.C. 112 1st for lack of enablement. Specifically, given the combination of factors of record, it would have required undue, unpredictable experimentation for one of skill in the art to use the claimed polypeptides. For example, in order to determine whether the a polypeptide meeting the claim limitations of a given percent identity to SEQ ID NO: 255, or portions thereof, has a particular activity one would have to envision an appropriate assay and conditions for measuring the purported activity. With proteolytic activity, one of skill in the art would have to envision which possible substrate of all the possible protein substrates available and under which conditions would be likely to result in an observation of the supposed activity. One would then have to envision the appropriate reaction conditions for performing the assay (e.g. purified or unpurified protein, temperature, buffer conditions, possible co-factors, etc.). If unsuccessful in determining an activity for the claimed protein, which is likely given the combination of factors outlined above and the unpredictability of the art, one of skill in the art would then have to envision a change to the first assay conditions (e.g. different substrate, buffer composition, temperature, duration and/or completely different assay) and repeat the entire unpredictable process. Thus, it would require undue, unpredictable

experimentation for one of skill in the art to use the claimed proteins having a specified percent identity to PRO302 (SEQ ID NO: 255). Therefore, the instant specification is not considered to be enabling for the use of any of the claimed proteins.

Response to Arguments

In response to the *prima facie* case and arguments of record, Applicant contends that, based on the data disclosed in the specification, the skilled artisan would know that PRO302 can be used as a target to develop therapeutic molecules that stop vascular leakage. Applicant concedes that the skilled artisan may need to conduct experiments to determine uses of anti-PRO302 *in vivo* such experimentation is not undue in view of the level of skill in the pertinent field at the time of filing.

This argument has been fully considered but is not deemed persuasive. In view of the fact that the disclosure fails to establish any role for the PRO302 in any particular pathological state, the skilled artisan would not know what condition to treat using therapeutic molecules developed therewith. The application teaches that some undisclosed amount of exogenously added PRO302 induces sufficient vascular permeability to be scored positive in a Guinea pig vascular leak assay and then asserts, based on this disclosure, that the skilled artisan would immediately recognize that the PRO302 polypeptide can be used to develop therapeutic molecules that stop vascular leakage. However, in order to further develop the invention such that it could actually be used to develop therapeutic molecules that stop vascular leakages, the skilled artisan would have to determine experimentally that the PRO302 polypeptide actually played a role in vascular leakage associated with pathological states and that the role played by PRO302 is pivotal such that

therapeutic molecules targeting the protein would actually have therapeutic efficacy. The amount of experimentation required is clearly beyond what would be considered routine, regardless of the level of skill in the art, because it requires that the skilled artisan establish that the claimed invention is actually a viable target for therapeutic intervention.

Applicant is reminded, "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Genentech Inc. v. Novo Nordisk A/S CA FC) 42 USPQ2d 1001, 1005.

Applicant's arguments and the showings of the declaration have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure.

Claim Rejections - 35 USC § 112, first paragraph, written description

Claims 42, 43, 50 and 51 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention for reasons of record and herein below.

Response to Arguments

In response to the *prima facie* case, set forth in the 26 February Office Action, and arguments of record, Applicant resubmits, *verbatim*, the arguments filed 14 December 2004 (page 6). These arguments were fully addressed in the Office Action mailed 18 January 2005, the substance of which is reiterated herein below.

The written description guidelines are just that, guidelines. Each example from the guidelines is not meant to set an absolute standard for meeting the description requirement that can be stretched to fit every fact pattern for every application. For example, the instant claims recite variants of an ~450 amino acid protein that can vary by as much as 5% over the entire length of the protein, and which must retain the recited activity of enhancing vascular leakage. This encompasses a change of up to ~22 amino acid residues at any point in the polypeptide. Given the fact that such changes include additions, deletions and substitutions with up to 19 different amino acids at any given residue, the number of variants encompassed by the claimed genus of variants is incalculable. The instant specification does not describe a single variant that retains the recited activity. Nor does the specification provide any guidance as to what residues or domains within the protein are required for the recited activity. Thus, the specification provides no basis for the skilled artisan to envision which proteins encompassed by the structural limitations of the claims necessarily meets the functional limitations. For these reasons, the

skilled artisan could not have envisioned a sufficient number of protein variants of SEQ ID NO: 255 that meet the functional limitations of the claims to describe the broadly claimed genus.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §112, first paragraph, as lacking adequate descriptive support.

Claim Objections

Claims 42 and 43 are objected to because of the following informalities: The claims still recite the dependency from claim 39, although claim 39 has been canceled. Amending the claims to recite, "An isolated polypeptide having..." would be remedial. Appropriate correction is required.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

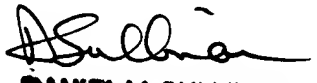
however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.
Examiner
Art Unit 1636



DANIEL M. SULLIVAN
PATENT EXAMINER